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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,534	08/28/2000	Sylviane Gabrielle Nadine Dennler	1430-245	4173
20462	7590	06/29/2004	EXAMINER	
SMITHKLINE BEECHAM CORPORATION CORPORATE INTELLECTUAL PROPERTY-US, UW2220 P. O. BOX 1539 KING OF PRUSSIA, PA 19406-0939			YAEN, CHRISTOPHER H	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 06/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/601,534	Applicant(s) DENNLER ET AL.	
	Examiner Christopher H Yaen	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-21 is/are pending in the application.
- 4a) Of the above claim(s) 7-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

RE: Dennler *et al*
Priority Date: 6 February 1998

1. The amendment filed 4/7/2004 is acknowledged and entered into the record. Accordingly, claim 5 is canceled. Claims 1-4, and 6-21 are pending, claims 7-21 are withdrawn from further consideration as being drawn to a non-elected invention.
2. Claims 1-4 and 6 are therefore examined on the merits.

Claim Rejections Maintained - 35 USC § 102

3. The rejection of claims 1-3 under 35 USC 102 (e) as being anticipated by Laughon *et al* (US Patent 6,046,165) is maintained for the reasons of record. Applicant argues that the cited reference does not anticipate the instant invention because it "does not identically show every element of the claimed invention, and because it does not enable the instantly claimed invention." Applicant further argues that the cited reference differs from the instant invention because the instant specification "provide evidence that their recited oligonucleotide is functional in a more physiological system", and concludes that the cited reference is not enabling. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). Further, In the instant case, the cited reference provides all the elements of the claimed

invention (see in particular col. 21, lines 18-21 and figure 5 and its description).

Applicant's arguments regarding non-enablement is not persuasive because all prior art references are presumed to be enabling unless the applicant is able to rebut the operability of the reference, of which no such rebuttal is provided. A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

Applicant further argues that the sequence motif that is critical to Laughon *et al* is GCCGnCGc (SEQ ID No: 9), while that of the instant invention is a Smad binding element of sequence AG(C/A)CAGACA. Applicant further argues that the sequence taught by Laughon *et al* are "longer than those used by the Applicants, a fact that could change the results of transcriptional screens used to identify "agents", and further states that "Laughon does not disclose the exact oligonucleotide recited by the instant claims." Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. The claims of the instant invention are drawn to a method wherein the oligonucleotide comprises the claimed motif. As stated in the prior office action, SEQ ID No: 10 and 11 both comprise the claimed motif as specifically recited in the claim. Furthermore, whether the sequence is "longer" and could "change the results" is speculation and is not supported with any factual evidence to rebut the anticipation of Laughon *et al*. Therefore the rejection of the claims are maintained.

New Arguments

Specification

4. The disclosure is objected to because of the following informalities: The specification contains sequences that are not identified by sequence numbers (see page 20 and 21 for example). Applicant must amend the specification to comply with the sequence rules as set forth in 37 CFR 1.821, see MPEP 2400.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

5. Claims 1-4, and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. With regard to claims 1 and 6 in particular, the claims recite the terms "Smad2", "Smad3", and "Smad4" as the sole means of identifying the claimed molecules. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify "Smad2", "Smad3", and "Smad4", for example, by SEQ ID NO. and function of "Smad2", "Smad3", and "Smad4".

Claim Rejections - 35 USC § 112, 1st paragraph

7. Claims 1-4 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

The specification of the instant invention defines the "Smad2, "Smad3", and "Smad4" proteins as that defined by Heldin *et al* (Nature 1997; 390:465-471) – see page 1 and 2 of the specification. However, because the "Smad2, "Smad3", and "Smad4" proteins are considered critical to the practice of the instant invention, the incorporation of essential material by reference to non-patent literature is improper.

The following is noted.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112; however this does not bar incorporation by reference. Ex parte Schwarze, 151 USPQ 426 (Bd. of Appeals, 1966). an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Nonessential subject matter may be incorporated by reference to (1) patents or application published by the United states or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications or (3) non-patent publications, for purposes of indicating the background of the invention or illustrating the state of the art.

The referencing application must include (1) an abstract, (2) a brief summary of the invention, (3) an identification of the referenced patent or application, (4) at least one view in the drawing in those applications admitting of a drawing, and (5) one or more claims. Particular attention should be directed to specific portions of the referenced patent or application.

Applicant is reminded to provide a Sequence Listing which complies with the requirements of 37 CFR 1.821 through 1.825 for Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is reminded to provide the appropriate Hawkins Declaration to accompany amending the instant specification to provide the essential subject of the amino acid sequences defining the claimed "Smad2, "Smad3", and "Smad4", as set forth by Heldin *et al* (Nature 1997; 390:465-471).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 1-3 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laughon *et al* (US Patent 6,046,165).

- a. The teachings of Laughon *et al* (US Patent 6,046,165) are set forth above as applies to claims 1-3.
- b. Laughon *et al* do not specifically teach a kit comprising at least one Smad protein; a TGF- β or activin; and a double stranded DNA molecule comprising a sequence of the motif 5' WXYCAGACZ 3'.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a kit comprising the components listed above (see item "b", *supra*) because all the components of the claimed kit were already taught by Laughon *et al* (see in particular col. 21, lines 18-21 and figure 5 description and SEQ ID No: 10 and 11). One of skill in the art would have been motivated to combine the components into a kit because the components were already taught as being effective in screening for "agents" and must be combined and hence found in separate containers. The combination of the containers into a single kit would provide for an easy means to replicate the screening process already taught by Laughon *et al*. One of skill in the art would expect a reasonable amount of success in combining the components because Laughon *et al* has already taught that the separate components are required in order for the screening process to function.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 4/7/2004.

Conclusion

10. No claim is allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

Art Unit: 1642

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
June 17, 2004


GARY NICKOL
PRIMARY EXAMINER